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Short Communication

Estimation of the secondary attack rate of COVID-19 using proportional meta-analysis of nationwide contact tracing data in Taiwan



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KEYWORDS

COVID-19; Secondary attack rate; Meta-analysis; Pandemic; Bayesian Abstract Crude secondary attack rate (SAR) of COVID-19 in Taiwan was 0.84% using nation-wide contact-tracing data till April 8, 2020. The random-effect Bayesian metaanalysis yielded 95% credible intervals of 0.42%—1.69% and 0.08%—8.32%, respectively, for estimated SAR pooling from 15 case series and for predicted SAR in the future if pandemic continues. Copyright © 2020, Taiwan Society of Microbiology. Published by Elsevier Taiwan LLC. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Pandemic of coronavirus disease 2019 (COVID-19) originated from person-to-person transmission. Epidemiological studies in several aspects, including the transmissibility of

severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) of COVID-19, are urgently needed for setting containment strategies. Secondary attack rate (SAR) is the

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probability that an infection occurs among susceptible persons within a reasonable incubation period after known contact with an infectious person in household or other close-contact environments. SAR can be influenced by many factors including personal hygiene habits, social behaviors, and characteristics of close-contact environments.

Up till now, there have been only few studies reporting an estimate SAR of COVID-19 with a wide range from 0.46% to 63.87%. 1-4 These studies used cases or cases series with relatively small sample size in a specific close-contact setting such as during meal, household or travel-related environments. Instead of a specific setting, estimation of SAR using data from multiple close-contact environments is more valuable for describing the overall burden and evaluating the effectiveness of the containment approaches. 1 It is known that case reports and case series are study designs known for increased risk of bias, and meta-analysis is considered as an appropriate approach to attain a weighted average of results from such studies. Proportional metaanalysis has been used previously to estimate SAR of emerging infectious disease such as H1N1 Influenza A and Ebola Virus. 6,7 Considering the heterogeneity among close contact environments of secondary cases, we used the nationwide contact tracing data from the Centers for Disease Control (CDC) in Taiwan and performed proportional meta-analyses to estimate SAR of COVID-19.8

In the world, only Taiwan Central Epidemic Command Center (CECC) announces daily report of contact tracing data regarding susceptible individuals who had close contact with imported or indigenous confirmed COVID-19 cases. We collected these data during January 21st, 2020 to April 8th, 2020 from Taiwan CDC. Only closing follow-up cases with complete surveillance more than 14 days were enrolled. A total of 3795 individuals who were closely contacted with primary confirmed cases were registered and monitored under tracing and/or quarantine. These individuals were screened for positive of SARS-CoV-2 by reverse-transcription diagnostic polymerase chain reaction tests. We calculated the crude SAR with the formula of "number of secondary confirmed cases/number of susceptible cases." We then performed proportional metaanalyses by Bayes' theorem to estimate the pooled SAR based on the current data and to predict SAR in the future if pandemic continues.

Among 3795 susceptible individuals who had close contact with primary confirmed cases, 32 cases were later confirmed to be SARS-CoV-2 positive (Table 1). The close contact environments included household, aircraft, school classroom, hospital, and working places. Based on these data, the value of crude SAR calculation was 0.84%. We furthermore undertook the Bayesian random effect metaanalysis by using software WinBUGS with Markov chain Monte Carlo methods, noninformative priors, and 3 chains with 150,000 simulations. By pooling the proportion of 15 case series, the median of estimated SAR was 0.88% (95% Credible Interval [CrI]: 0.42%-1.69%; Fig. 1). This interval denotes the possible range of SAR based on past data in Taiwan included in our analysis. One advantage of the Bayes' theorem is to forecast the post probability based on evidence of current efforts, the estimated SAR from the announced case series, as prior. 9 It can provide a predicted SAR in the future if the pandemic continues its progress and

| Table 1 Environments of secondary attacks. | | | |
|--|---------------|------------|---------------|
| Primary | Number of | Number of | Environments |
| confirmed | susceptible | confirmed | for close |
| cases with | persons with | cases with | contact |
| serial | close-contact | secondary | |
| numbera | tracing | attack | |
| Case 1 | 274 | 1 | Aircraft |
| Case 2 to 10 | 203 | 2 | Household |
| Case 19 | 256 | 4 | Dinning and |
| | | | household |
| Case 24 | 853 | 2 | Household |
| Case 27 | 828 | 5 | Household |
| | | | and hospital |
| Case 34 | 455 | 8 | Hospital |
| Case 39 | 69 | 1 | Classroom |
| Case 59 | 57 | 2 | Classroom |
| Case 84 | 29 | 1 | Household |
| Cases in a | 108 | 1 | Household |
| tour | | | |
| group ^b | | | |
| Case 160 | 41 | 3 2 | Working place |
| Case 277 | 24 | 2 | Working place |
| | | | and |
| | | | household |

^a Serial numbers of primary confirmed cases were defined by Taiwan Centers for Disease Control.

spreads to community, and yielded a predicted median SAR of 0.88% (95% CrI: 0.08%—8.32%).

In prior reports of COVID-19 SAR from different countries and environments, data were all collected at the early stage of COVID-19 pandemic. In United State, one study reported 12 travel-related COVID-19 cases under condition of hospital or household isolation immediately after immigration and monitoring of active symptoms was performed on 445 close contacts.³ The results showed symptomatic cases with SAR of 0.45% (95% confidence interval [CI]: 0.12%-1.6%) among all contacts, and 10.5% (95% CI: 2.9%-31.4%) among household members.3 However, such situation with a low SAR was far different from that of the or country-based prevention community-based pandemic. In South Korea, one study reported first 30 confirmed cases as of February 17th 2020, and 13 individuals of 2370 traced contacts were infected. The overall and household SAR were 0.55% (95% CI: 0.31%-0.96%) and 7.56% (95% CI: 3.73%-14.26%), respectively.⁴ The low SAR reported in this study stand for the beginning of COVID-19 outbreak. There was no more available data of contact tracing after the first 30 cases because the government of South Korea shifted the policy from contamination to mitigation. 4 Low SAR of COVID-19 in our results based on multiple close-contact environments with duration of three months represented different significance in epidemiology.

The value of crude SAR could be easily influenced by different contacts. However, our data regarding crude SAR still lines within the ranges calculated by our meta-analytic

^b Case 55, 63, 71, 101, 111, 140, 161, and 162 joined the same tour group to Egypt and were confirmed when back to Taiwan.

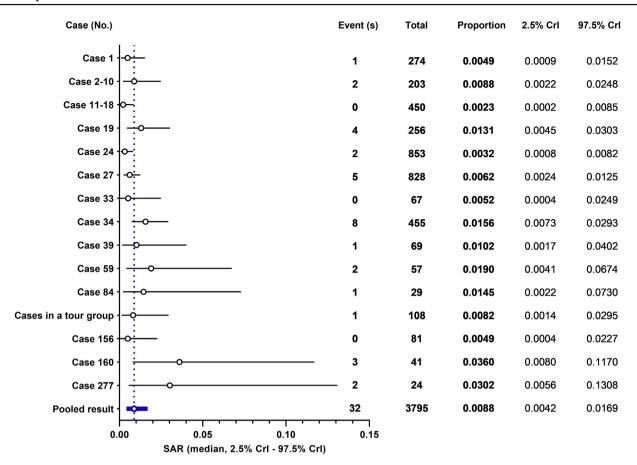


Figure 1. Results of meta-analysis for estimation of secondary attack rate (SAR) of coronavirus disease 2019 (COVID-19) using nationwide contact tracing data in Taiwan. The result from the random effect of Bayesian model is presented. This analysis included data during the period from January 21st, 2020 to April 8th, 2020 were obtained from Taiwan Centers for Disease Control. Event (s), secondary confirmed cases after close contact with primary confirmed cases; total, all contact tracing cases who exposed to primary confirmed cases; CrI, credible interval. Details of the close contact environments for each case of group are listed in Table 1.

model. The results indicated that the containment of COVID-19 pandemic in Taiwan remained consistent in the past three months. The low SAR of COVID-19 in Taiwan may result from the effective strategic approaches implemented by CECC, including inspecting imported passengers with symptoms, monitoring quarantined individuals by government-issued cell phones, the efficient distribution of facial masks to people in need, and discouraging mass gathering. The high awareness and cooperation of the whole population, especially regarding hand washing and mask wearing, also plays an important role. Most importantly, the value of SAR might stay low in the future, according to the prediction by Bayes' theorem in our study.

Nosocomial spread of SARS-CoV-2 is a critical issue in curbing the pandemic progress, not only to hospitalized patients but also to medical staffs. In our result, the estimate of SAR for the Case 34 yielded a median of 1.56% with 95% CrI of 0.73%—2.93% because of intra-hospital transmission. These data are valuable because this may be the first report of nosocomial COVID-19 SAR. The challenge for clinical staffs is that COVID-19 cannot be distinguished from other causes of pneumonia merely by clinical, radiologic or laboratory information. Besides, nosocomial

transmission from asymptomatic carriers is possible. ¹¹ In 2003, SARS demonstrated a high nosocomial transmission, which gave more than 56% of attack rate among health care workers. ¹³ Thus, the relatively very low nosocomial COVID-19 SAR in Taiwan should be because extensive training and high-degree awareness of clinical staffs learned from the experience of SARS.

In conclusion, the SAR of COVID-19 in Taiwan was low and consistent during January 21st, 2020 to April 8th, 2020. Based on the good results, Taiwan's experience is worth offering these strategies worldwide to reduce SAR of COVID-19.

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Declaration of Competing Interest

None.

References

- Liu Y, Eggo RM, Kucharski AJ. Secondary attack rate and superspreading events for SARS-CoV-2. Lancet 2020;395:e47. https://doi.org/10.1016/S0140-6736(20)30462-1.
- Sun WW, Ling F, Pan JR, Cai J, Miao ZP, Liu SL, et al. Epidemiological characteristics of 2019 novel coronavirus family clustering in Zhejiang Province. Zhonghua Yufang Yixue Zazhi 2020; 54:E027. https://doi.org/10.3760/cma.j.cn112150-20200227-00199.
- Burke RM, Midgley CM, Dratch A, Fenstersheib M, Haupt T, Holshue M, et al. Active monitoring of persons exposed to patients with confirmed COVID-19 - United States, January-February 2020. MMWR Morb Mortal Wkly Rep 2020;69:245—6. https://doi.org/10.15585/mmwr.mm6909e1.
- COVID-19 National Emergency Response Center. Epidemiology and case management team, Korea centers for disease control and prevention. coronavirus disease-19: summary of 2,370 contact investigations of the first 30 cases in the Republic of Korea. Osong Public Health Res Perspect 2020;11:81–4. https: //doi.org/10.24171/j.phrp.2020.11.2.04.
- Murad MH, Sultan S, Haffar S, Bazerbachi F. Methodological quality and synthesis of case series and case reports. *BMJ Evid Based Med* 2018;23:60—3. https://doi.org/10.1136/bmjebm-2017-110853.
- Glatman-Freedman A, Portelli I, Jacobs SK, Mathew JI, Slutzman JE, Goldfrank LR, et al. Attack rates assessment of the 2009 pandemic H1N1 influenza A in children and their contacts: a systematic review and meta-analysis. *PloS One* 2012;7:e50228. https://doi.org/10.1371/journal.pone.0050228.

- Dean NE, Halloran ME, Yang Y, Longini IM. Transmissibility and pathogenicity of Ebola virus: a systematic review and metaanalysis of household secondary attack rate and asymptomatic infection. Clin Infect Dis 2016;62:1277–86. https: //doi.org/10.1093/cid/ciw114.
- Taiwan Centers for Disease Control. Daily press release of COVID-19. available from: https://www.cdc.gov.tw/En. [Accessed 21 April 2020].
- López Puga J, Krzywinski M, Altman N. Points of significance: bayes' theorem. Nat Methods 2015;12:277–8. https://doi.org/10.1038/nmeth.3335.
- Wang CJ, Ng CY, Brook RH. Response to COVID-19 in Taiwan: big data analytics, new technology, and proactive testing. *J Am Med Assoc* 2020;323:1341–2. https://doi.org/10.1001/jama.2020.3151.
- 11. Lai CC, Liu YH, Wang CY, Wang YH, Hsueh SC, Yen MY, et al. Asymptomatic carrier state, acute respiratory disease, and pneumonia due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): facts and myths. *J Microbiol Immunol Infect* 2020; 53(3):404—12. https://doi.org/10.1016/j.jmii.2020.02.012.
- 12. Huang WH, Teng LC, Yeh TK, Chen YJ, Lo WJ, Wu MJ, et al. 2019 novel coronavirus disease (COVID-19) in Taiwan: reports of two cases from Wuhan, China. *J Microbiol Immunol Infect* 2020. https://doi.org/10.1016/j.jmii.2020.02.009.
- World Health Organization. 12. The weekly epidemiological record (WER), vol. 78; 21 March 2003p82. available from: https://www.who.int/wer/2003/en/wer7812.pdf. [Accessed 31 May 2020].